# PsA Therapeutic Arsenal Adds a Third TNF-Blocker

## *Adalimumab significantly improved joint and skin manifestations and inhibited structural changes.*

BY BRUCE K. DIXON
*Chicago Bureau*

A third tumor necrosis factor inhibitor has been added to the arsenal of drugs approved for treating psoriatic arthritis.

Adalimumab, a fully human, anti-TNF monoclonal antibody, significantly improved joint and skin manifestations, inhibited structural changes on radiographs, lessened disability due to joint damage, and improved quality of life in patients with moderately to severely active psoriatic arthritis, according to the findings of multicenter study.

Adalimumab and infliximab have been approved by the Food and Drug Administration for the treatment of psoriatic arthritis (PsA), but not for the dermatologic treatment of psoriasis in the absence of joint involvement. A third TNF inhibitor, etanercept, is approved for both PsA and the severe plaque of psoriasis.

In the study that served as the basis for the FDA approval of adalimumab for PsA, patients were stratified according to methotrexate use (yes or no) and degree of psoriatic involvement, and then randomized in a 1:1 ratio by site to receive either drug or placebo.

Of the 315 patients randomized to receive treatment, 162 were assigned to the placebo group and 153 were assigned to self-injected adalimumab 40 mg every other week. All patients who completed the 24-week protocol were eligible for long-term treatment in an open-label extension study.

The trial, which was conducted at 50 sites in the United States, Canada, and Europe, showed that patients treated with adalimumab achieved significantly higher American College of Rheumatology (ACR) response rates than those treated with placebo at all time points.

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**DR. MEASE**

"At week 12, the ACR20 response rate was 58% for the adalimumab treatment group and 14% for the placebo-treated group," study leader Philip J. Mease, M.D., of the Swedish Medical Center in Seattle, and his colleagues reported (Arthritis Rheum. 2005;52:3279-89).

"At week 24, the ACR 20 response rates were 57% and 15%, respectively. At 12 and 24 weeks, the ACR50 response rates were significantly higher in the adalimumab arm than in the placebo arm, and a significant difference in ACR 70 responses was also evident," they said, adding that ACR responses developed rapidly, "with statistically significant between-group differences in the ACR20 and ACR50 responses observed at week 2"; 27% vs. 6% achieving ACR20 and 11% vs. 0% achieving ACR50. At week 4, 7% vs. 1% achieved ACR70.

Across the board, response rates did not differ between patients taking adalimumab in combination with methotrexate and those taking the TNF inhibitor alone.

The mean change in the modified total Sharp score in patients who had both baseline and week 24 radiographs was –0.2 for those on adalimumab compared with 1.0 for those receiving placebo injections (*P* less than .001), "implying that protection against progressive structural damage was achieved," Dr. Mease said.

"Improvements seen in the skin manifestations of the disease were significant and occurred rapidly, results that were as good as or in some cases superior to results seen with other biologics," Dr. Mease told this newspaper. "At week 24, PASI [psoriasis area and severity index] showed a 75% improvement in 16% of adalimumab-treated patients, compared with only 3% of placebo patients (*P* less than .001).

Similarly, the physician's global assessment of psoriasis resulted in ratings of the lesions as "clear" or "almost clear" in 67% of the 70 adalimumab-treated patients evaluated, compared with only 10% of the 70 placebo-treated patients evaluated for psoriasis (*P* less than .001).

"It appears that the response was a little faster in the skin with adalimumab, as has also been seen with infliximab, than with other biologics. When it comes to joint symptoms and important aspects such as quality of life, physical function, and inhibition of progressive joint damage, the three anti-TNF drugs are similar; but if you have a patient with really severe skin disease, there may be a slight advantage to using either infliximab or adalimumab," Dr. Mease said.

The ink had hardly dried on this study when, in October, the FDA approved adalimumab for the treatment of PsA. "With etanercept, the PsA indication came ahead of the psoriasis indication, and the same is going to be true of adalimumab; that indication will likely follow once the pure psoriasis trials are fully considered by the FDA," said Dr. Mease.

The cost of etanercept and adalimumab, when used for RA or PsA in the standard dose of 50 mg per week and 40 mg every other week, respectively, is similar, he said. "The comparative costs of these agents in psoriasis have yet to be fully understood, and ultimately will depend upon the dosages used to achieve optimal effects in the skin."

Adalimumab was generally well tolerated during the 24-week trial. Common side effects "were similar to those seen in clinical trials involving patients with RA or were thought to be related to underlying disease," according to the authors.

Serious adverse events were experienced by 12 patients, including 7 in the placebo group and 5 in the adalimumab group. In the latter, events included nasal septum disorder, toe arthrodesis, aggravation of convulsions, viral meningitis (attributed to West Nile virus) and renal calculus; most of these were considered unrelated to the study medication.

The authors stress that longer-term follow-up from the open-label extension study is needed to confirm these results. The study was supported by Abbott Laboratories.

Dr. Mease has received consulting fees or honoraria of less than $10,000/year from Abbott. ■

# Adding Low-Dose Prednisolone Slows Early RA Progression

BY CHRISTINE KILGORE
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Low doses of prednisolone given for 2 years along with disease-modifying antirheumatic drug therapy substantially and safely reduced radiographic progression of rheumatoid arthritis in patients with early, active disease, according to the results of two new randomized studies.

Investigators of the two studies say that their findings support the use of low-dose daily prednisolone as a low-risk adjunct to DMARDs in patients with early RA.

One study compared the addition of 7.5 mg/day prednisolone to initial DMARD therapy (either methotrexate or sulfasalazine) with DMARD therapy alone in 250 patients recruited in six centers throughout Sweden from 1995 to 1999. The patients had had RA for 1 year or less.

Patients in the second study were randomized to receive placebo or an even smaller dose of prednisolone—5 mg/day—in addition to therapy with either gold sodium thiomalate or methotrexate.

The 103 patients who completed this study had a slightly longer disease duration—2 years or less—when they started treatment.

They were enrolled in the study between 1993 and 1995 in 20 clinics and private practices in Germany, Austria, and Switzerland.

The two studies were similar in that the choice of DMARD therapy was left to the treating physician. There were no significant differences, however, in the types and dosages of DMARD therapy between the patients who were randomized to receive prednisolone and those who received placebo or no prednisolone.

Concomitant treatment with NSAIDs and osteoporosis prophylaxis with calcium was allowed in both studies, and patients with any history of treatment with DMARDs or glucocorticoids were excluded. Joint destruction was monitored in both studies primarily through radiographs of the hands and feet.

The Swedish investigators used the Sharp score as modified by van der Heijde to assess radiographs at baseline and after 1 and 2 years of treatment. The change in the total score, they found, was significantly lower after 1 and 2 years in the prednisolone group than in the no-prednisolone group. (At 2 years, for instance, the median interquartile change in total score was 1.8 and 3.5, respectively.)

The erosion score also changed significantly less in the prednisolone group, and joint space narrowing was retarded, though to a lesser extent than erosion.

Patients in the prednisolone group also had significantly fewer newly eroded joints after 2 years, as well as improved physical functioning and significantly higher rates of disease remission (51% vs. 39% in the no-prednisolone group at 1 year, and 56% vs. 33% at 2 years), reported Björn Svensson, M.D., Ph.D., of the University of Lund (Sweden), and his associates (Arthritis Rheum. 2005:52;3360-70).

Investigators in the multicountry study used two scoring systems—the Ratingen score and the modified Sharp/van der Heijde score—to assess radiographs taken at 6 months, 1 year, and 2 years after the start of treatment.

Their results were similar: Increases in the Ratingen score, the Sharp score for erosion, and the total Sharp score were significantly less at each point in time in patients taking prednisolone than in patients taking placebo. Changes in the score for joint space narrowing were significantly different only at 6 months.

In addition, clinical and functional outcomes, as well as rates of disease remission, tended to be better—though not to the level of statistical significance—in the prednisolone group, reported Siegfried Wassenberg, M.D., of Evangelisches Fachkrankenhaus Ratingen (Germany), and his associates (Arthritis Rheum. 2005:52;3371-80).

Some side effects such as weight gain (four patients), hypertension (six), Cushing's syndrome (five), and glaucoma (three) were reported only among patients taking prednisolone.

In the Swedish study, the frequency of adverse events was small, investigators said. And in both studies, prednisolone had little or no impact on bone loss.

"It remains to be seen whether dosages lower than 5 mg provide the same benefit with even fewer side effects and whether the same effect can be produced in patients with more advanced disease," Dr. Wassenberg and associates said. ■